Bilateral versus single internal thoracic coronary artery bypass grafting: the ART RCT

Marcus Flather,[1*] Arnaldo Dimagli,[2,3] Umberto Benedetto,[2] Belinda Lees,[4] Alastair Gray,[5] Stephen Gerry,[6] Ajita Naik,[3] Jo Cook,[7] Mario Gaudino,[3] Matthew Little[5] and David P Taggart[4]; on behalf of the ART Investigators

[1]Norwich Medical School, University of East Anglia and Norfolk and Norwich University Hospital, Norwich, UK
[2]School of Clinical Sciences, University of Bristol and Bristol Royal Infirmary, Bristol, UK
[3]Department of Cardiothoracic Surgery Weill Cornell Medicine New York – Presbyterian Hospital, New York, USA
[4]Nuffield Department of Surgical Sciences, University of Oxford, John Radcliffe Hospital, Oxford, UK
[5]Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK
[6]Centre for Statistics in Medicine, Botnar Research Centre, University of Oxford, Oxford, UK
[7]Surgical Intervention Trials Unit, Botnar Research Centre, University of Oxford, Oxford, UK

[*]Corresponding author m.flather@uea.ac.uk

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Scientific summary

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Objectives

The Arterial Revascularisation Trial (ART) was a superiority trial aimed at comparing the outcomes of patients undergoing coronary artery bypass grafting (CABG) with either a bilateral internal thoracic artery (BITA) or single internal thoracic artery (SITA). The main secondary questions were whether using multiple arterial grafting (MAG) was associated with improved clinical outcomes and whether additional factors influence the efficacy of MAG such as diabetes and age.

Methods

Patients with multivessel coronary artery disease (CAD) involving at least the left anterior descending artery and the circumflex artery undergoing CABG were included and randomised equally to BITA or SITA. Emergency patients (refractory myocardial ischaemia/cardiogenic shock) and those requiring single grafts or redo CABG were excluded. After surgery, patients were followed-up on annual basis. Based on power calculation, 2928 patients were needed to be enrolled to detect an absolute 5% difference in mortality between the two groups with 90% power at the 5% significance level.

The primary outcome of the trial was all-cause mortality and the secondary outcomes were the composite of death from any cause, myocardial infarction (MI), or stroke (in a time-to-event analysis), rate of repeat revascularisation and safety outcomes (including bleeding and sternal wound complications).

The primary research question used the log rank method to compare survival in the BITA and SITA groups based on the intention to treat principle and censored patients at 10 years of follow-up after the date of randomisation. Secondary analyses used the as-treated principle and applied propensity score-based methods as appropriate to reduce confounding.

Results

A total of 3102 patients were enrolled in the trial: 1548 received BITA and 1554 SITA. Complete follow-up data for the primary outcome were available for 98% of patients at 10 years. Aspirin was used in 80%, beta-blockers 74%, statins 90% and angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers in 71%. The death rate at 10 years was 20.3% in the BITA group and 21.2% in the SITA group [hazard ratio (HR) 0.96; 95% confidence interval (CI) 0.82 to 1.12; $p = 0.62$] while the composite of all-cause mortality, MI or stroke occurred in 24.9% in BITA compared with 27.3% in SITA (HR 0.97; 95% CI 0.83 to 1.14; $p = 0.12$). In those randomised to BITA, 86% actually received BITA grafts while in the SITA group, 97.5% received SITA. Additional radial artery grafts were used in 19% of patients in BITA and 22% in SITA.

In a secondary analysis exploring the effect of multiple (MAG) and total arterial grafting (TAG), there was a significant trend toward a reduction in 10-year mortality in the MAG and TAG groups compared with single arterial grafting (SAG) (test for trend = 0.04). TAG was associated with a reduction in all-cause death when compared with SAG ($P = 0.03$). The benefit of TAG was also confirmed for the composite endpoint including death, MI, stroke or repeat revascularisation ($P = 0.02$) compared with SAG.

When investigating the effect of diabetes, MAG was associated with a survival benefit in both the diabetic and non-diabetic groups compared with SAG. Similarly, MAG was associated with lower rates of

the composite endpoint of death, MI and stroke in the diabetic and non-diabetic groups. However, MAG was associated with higher rates of deep sternal wound infection compared with SAG in both the diabetic and non-diabetic groups. Patients with insulin-dependent diabetes receiving MAG experienced the highest absolute rate of sternal wound infection (9.6%). Use of BITA was found to be associated with higher rates of sternal wound infection.

Limitations

The elevated crossover rate between BITA and SITA and the non-randomised use of RA grafts may have contributed to a loss of power to detect a difference in mortality between the two groups. Moreover, secondary analyses are prone to bias as they compare non-randomised groups.

Conclusions

The ART has shown that is possible to run pragmatic long-term trials in cardiac surgery. Overall, the study has not shown that use of BITA is associated with reduced mortality compared to SITA. Secondary analyses support the potential benefit of MAG and TAG. More information is needed to understand the interaction of graft patency and clinical outcomes after CABG, and routine computed tomography coronary angiography may be a useful option.

Trial registration

This trial is registered as ISRCTN46552265.

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